

AMENDMENTS TO THE SPECIFICATION:

Page 1, replace the last paragraph as follows:

--Multiple drug resistance of infectious agents and particularly of bacteria to antibiotics such as ~~penicillins~~ penicillins,  $\beta$ -lactamines, cephalosporines, aminoglycosides, macrolides and sulfamides, is more and more often seen in hospitals.--.

Page 2, replace the first paragraph as follows:

--Monocyte derived cells (MDCs) are immune cells such as obtained by culture of blood mononuclear cells in non adherent gas permeable plastic or Teflon bags for 5 to 10 days at 37°C in O<sub>2</sub>/CO<sub>2</sub> atmosphere. Their culture medium (RPMI, IMDM, AIM5 (Gibco) or X-VIVO (Biowhittaker)) contains eventually cytokines or ligands as defined in patents n° PCT/EP93/01232, n° WO94/26875 or EP 97/02703 or in the articles mentioned below:--;

replace the paragraph beginning on line 24 as follows:

--They can be activated by ~~INF- $\gamma$~~  IFN- $\gamma$  at the end of culture to obtain in particular cytotoxic macrophages. They can be centrifuged to be concentrated and purified before resuspension in isotonic solution.--;

replace the last paragraph bridging pages 2 and 3 as follows:

--Monocyte derived cells (MDCs) can either be killer macrophages, phagocytosing cells, growth factors and cytokines releasing cells, or dendritic cells according to their conditions of differentiation. Dendritic cells can for example be obtained

as described in "In vitro generation of CD83<sup>+</sup> human blood dendritic cells for active tumor immunotherapy" (Thurnher M., Papesh C., Ramoner R., Gastlt G. and al.; Experimental Hematology, 25: 232-237, 1997) and "Dendritic cells as adjuvants for immune-mediated resistance to tumors" (Schuler G. and Steinman R. M.; J. Exp. Med., 186: 1183-1187, 1997), and EP #° 97/02703.--.

Page 3, replace the last paragraph as follows:

--This treatment can be conducted after first failure and relapse following chemotherapies, or before chemotherapy, to prevent chemoresistance. Local treatment with chemotherapy drugs causes cell necrosis and release of chemokines which call and actively ~~reerute~~ recruit macrophages and ~~monocytes~~ monocyte derived cells. Therefore, combining the chemotherapy with macrophage immunotherapy can in synergy increase cytotoxicity and increase immune response at the same time as preventing the establishment of resistance. Additionally to a first treatment combining conventional approach with immunotherapy, macrophage adoptive therapy can be proposed after failure and relapse.--.

Page 4, replace the fourth paragraph as follows:


--The active ingredients which are administered either at the same time, or separately, or sequentially, according to the invention, do not represent a mere aggregate of known agents, but a new combination with the surprising valuable property that immunotherapy with monocyte derived cells modifies the chemoresistance/chemosensitivity and allows a new effective treatment (partial or complete response) with similar chemotherapy

Application No. 09/647,529  
Amdt. dated July 21, 2003  
Preliminary Amendment  
Docket No. 0508-1011-1

~~protocole~~ protocol. Furthermore, synergy is observed between  
monocyte derived cells immunotherapy and chemotherapy.--.

Respectfully submitted,

YOUNG & THOMPSON



---

Robert J. Patch, Reg. No. 17,355

745 South 23<sup>rd</sup> Street  
Arlington, VA 22202  
Telephone (703) 521-2297

RJP/psf